Results of Extracorporeal Membrane Oxygenation (ECMO) Support before Coronary Reperfusion in Cardiogenic Shock with Acute Myocardial Infarction

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Background: Despite aggressive treatment, the mortality rate of cardiogenic shock with acute myocardial infarction (AMI) is high. We performed extracorporeal membrane oxygenation (ECMO) prior to coronary reperfusion, and evaluated the early clinical results and risk factors. **Materials and Methods:** From May 2006 to November 2009, we reviewed the medical records of 20 patients in cardiogenic shock with AMI (mean age 67.7±11.7 yrs, M : F 14 : 6). After initially performing ECMO using the CAPIOX emergency bypass system (EBS®Terumo, Tokyo, Japan), patients underwent coronary reperfusion (coronary artery bypass grafting, 13; percutaneous coronary intervention, 7). **Results:** All patients were in a cardiogenic shock state, cardiopulmonary resuscitations (CPR) were performed for fourteen patients (mean CPR time 20.8±26.0 min). The mean time from vascular access to the initiation of ECMO was 17.2±9.4 min and mean support time was 3.8±4.0 days. Fourteen patients were able to be weaned from ECMO and ten patients were discharged (mean admission duration 50.1±31.6 days). Patients survived on average 476.6±374.6 days of follow-up. Longer CPR and support time, increased cardiac enzyme, lower ejection fraction, lower albumin, and major complications were the risk factors of mortality (p＜0.05). **Conclusion:** The early application of ECMO prior to coronary reperfusion and control of risk factors allowed for good clinical results in cardiogenic shock with AMI.

Key words: 1. Extracorporeal membrane oxygenation (ECMO)
2. Coronary reperfusion
3. Acute myocardial infarction
4. Cardiogenic shock

INTRODUCTION

The mortality rate of cardiogenic shock due to my-ocardial infarction (AMI) is as high as 60～80% and may be higher without aggressive treatment. Besides the classical medical treatment, circulatory supportive devices such as the Intra Aortic Balloon Pump (IABP) and Ventricular Assistance Device (VAD) may be helpful [1-5]. Recently ECMO has

been adapted to the percutaneous approach and the self-charging system, so that it can support the whole body and coronary circulation fast, and has shown good clinical results in patients experiencing cardiogenic shock due to AMI [6-9]. On the other hand, there is controversy about which procedure should be first, coronary reperfusion or ECMO, for cardiogenic shock due to AMI. Therefore, the authors have reviewed the short-term results of patients who had received ECMO just before coronary reperfusion in cases of cardiogenic shock due to AMI.

MATERIALS AND METHODS

We retrospectively reviewed 20 cases (median age 67.7±11.7, male : female 13 : 7) of coronary reperfusion after application of EBS (Capiox® Emergency Bypass System [Terumo Inc., Tokyo, Japan]) due to postinfarct cardiogenic shock among 106 cases of ECMO from February 2005 to November 2009. We defined a state of cardiac arrest, systolic blood pressure below 70 mmHg for over 30 minutes and clinical symptoms such as oliguria, confusion, and ventricular tachycardia as cardiogenic shock. We applied ECMO to those patients experiencing cardiogenic shock and performed CPR in 14 of the cases (70%) (mean time 20.8±26.0 minutes). In all cases, we underwent coronary artery bypass under the support of ECMO and chose the method of coronary reperfusion according to the results. After using ECMO support, arterial pulse wave was disappeared in 14 cases, and in those cases we additionally inserted an IABP. Immediately after coronary reperfusion, we started Aspirin and Clopidogrel in all patients.

To perform ECMO, we inserted a 17 Fr cannula into the artery and 21 Fr cannula into the vein (Medtronic Inc.®, DLP, MN, USA) percutaneously using the Seldinger method and adjusted the size of cannulae according to the patient's body weight and body surface area. We infused with as much as 5,000 IU heparin before cannulation, and maintained an ACT (Activated Coagulation Time) in the range of 180 to 200 minutes. We maintained cardiopulmonary circulatory blood flow in the range of 3.0∼3.5 L/min/m^2 and stopped or lowered the vasopressor to the minimum dosage after ECMO support. During ECMO support, we performed echocardiography daily to check heart function and to check for any ventricular dilation or ventricular thrombus. We maintained platelet and hemoglobin counts over 50,000/μ and 10.0 gm/dL, respectively. During ECMO support, we employed continuous renal replacement therapy (CRRT) in cases of acute renal failure (ARF) by connecting CRRT unit to the ECMO circuit directly.

The weaning from ECMO was begun after the initial 48 hours from the application, raising the dosage of vasopressors and decreasing supportive circulatory blood flow. After weaning from ECMO, the cannula insertion sites were sutured after identification of the femoral artery intima in the Intensive Care Unit (ICU), and there were no complications from the cannula insertion site sutures.

We analyzed the risk factors using a 2×2×2 K Pearson's chi-square test and Fisher's exact test. We compared the mean values of the clinical results using a nonparametric Mann-Whitney U-test.

RESULTS

The mean cannular insertion time for ECMO application was 17.2±9.4 minutes, we performed peripheral circulation at the same time to prevent lower extremity from necrosis in two cases. The cannular insertions were performed in the coronary catheterization room in most cases (17 cases). Two cannular insertions were performed in the Emergency Room and one in the ICU.

Coronary angiography showed 11 cases of three-vessel diseases, 6 cases of two-vessel diseases, one case of single coronary disease and 6 cases of left main branch lesions. The main lesion was the left main branch in 5 cases, the left anterior descending artery in 4, the left circumflex artery in 6, and the right coronary artery in 5 cases. We decided the method of coronary reperfusion according to each patient's coronary angiography results and state. We performed 13 cases of coronary bypass graft surgery and 7 cases of Percutaneous Coronary Intervention (PCI). There were surgeries combined with coronary bypass graft surgery in 5 cases (mitral valvuloplasty in 2 cases, repair of a left ventricle rupture in one case, Dor procedure in one case, and repair of postinfarct ventricular septal defect in one case).

Table 1. Clinical results

	Total	Survivors (n=10)	Death (n=10)	p-value
ECMO support (hrs)	3.8±4.3	2.1±1.4	5.6±5.4	0.06
ICU stay (days)*	11.05±6.8	14.8±6.2	7.3±5.4	0.00
Admission duration (days)	28.75±31.1	50.1±31.6	7.4±5.3	0.01

*ICU=Intensive care unit.

Table 2. Pre ECMO risk factors

Variable	Weaning (n=14)	Failure (n=6)	p-value (OR[††])	Survivors (n=10)	Deaths (n=10)	p-value (OR)
Age (>70)				5	7	0.65
Sex (female)	11	3	0.30	7	7	1.00
DM*	5	2	1.00	3	4	1.00
Hypertension	6	3	1.00	4	5	0.50
Renal failure (Creatinine >1.6)	5	2	0.66	4	3	1.00
Culprit lesion (It)	4	1	1.00	7	8	1.00
Left main disease	4	2	1.00	3	3	1.00
3 vessel disease	7	3	1.00	4	6	0.656
IABP support[†]	11	3	0.30	7	7	1.00
CPR[†]	9	5	0.61	5	9	0.14
CPR time (20< min)	4	4	0.16	1	7	0.02 (21.0)
Cannula insertion time (<15 min)	8	1	0.16	5	4	1.00
Reperfusion (operation)	8	5	0.36	6	7	1.00
Ejection fraction (<30%)	5	4	0.14	2	7	0.02 (14.0)
Hematocrit (<30%)	2	3	0.13	2	3	1.00
CRP (0.5 mg/L>)[‖]	4	3	0.61	2	5	0.35
WBC (>10,000)	10	5	1.00	7	8	1.00
PH (<7.3)	6	2	1.00	4	4	1.00
AST (>100 U/L)[¶]	6	2	1.00	5	3	0.65
ALT (>100 U/L)[#]	2	2	0.55	2	2	1.00
NT proBNP (>500 pg/mL)[§]	8	4	0.26	5	7	0.29
Albumin (<3.0 g/dL)	5	5	0.14	2	8	0.01 (16.0)
Troponin I (>10 ng/mL)	3	2	0.61	2	3	1.00
CKMB (>10 ng/mL)**	5	4	0.33	4	5	1.00

*=Diabetes mellitus; [†]=Cardiopulmonary resuscitation; [†]=Intra aortic balloon pump; [§]=N-Terminal fragment of the prohormone, Brain-Type natriuretic peptide; [‖]=C reactive peptide; [¶]=Aspartate aminotransferase; [#]=Alanine aminotransferase; **=Creatin kinase MB; [††]=Odd ratio.

Mean ECMO support time was 3.8±4.3 days (0.5 to 19.2 days). Fourteen cases (70%) were weaned from ECMO and 10 patients (50%) were alive and discharged from the hospital. The mean length of hospitalization was 28.8±31.1 days (1 to 58 days) and mean time in ICU was 11.1±6.8 days (1 to 25 days) (Table 1).

The cause of death was failure of ECMO weaning in 6 cases, brain injury in 2 cases, restenosis of coronary artery in one case, and sepsis in one case. The causes of ECMO weaning failure were failure of left ventricular decompression in 2 cases, decrease of circulatory blood flow due to bleeding, and sepsis in 3 cases and heart dysfunction before ECMO support in one case. The main complications were sepsis and Disseminated Intravascular Coagulation (DIC) in 9 cases, acute renal failure in 9 cases, bleeding in 8 cases, and brain injury in 4 cases. We applied CRRT to 8 of the 9 cas-

Table 3. Risk factors during ECMO

Variable	Weaning (n=14)	Failure (n=6)	p-value (OR[¶])	Survivors (n=10)	Deaths (n=10)	p-value (OR)
Hematocrit (<26%)	7	5	0.33	4	8	0.17
Platelet count (<100,000)	4	4	0.16	3	5	0.65
Albumin (<2.5 g/dL)	6	5	0.16	3	8	0.07
PH (<7.3)	6	4	0.33	4	6	0.65
AST (>400 U/L)[*]	4	4	0.16	2	6	0.17
ALT (>100 U/L)[†]	5	4	0.33	4	5	1.00
ARF[†]	4	6	0.01	1	9	0.00 (81.00)
CKMB (>100)[§]	8	5	0.35	4	9	0.06
Troponin I (>100)	7	5	0.33	3	9	0.02 (13.50)
DIC[‖]	2	6	0.00 (5.00)	1	7	0.02 (21.00)
Bleeding	3	5	0.02 (18.33)	1	7	0.02 (21.00)
Sepsis	2	2	0.55	0	4	0.09
ECMO support time (>4.5 days)	3	3	0.30	0	6	0.01

[*]=Aspartate aminotransferase; [†]=Alanine aminotransferase; [†]=Incase creatininin over 50% of normal range; [§]=Creatin Kinase; [‖]=Disseminated intravascular; [¶]=Odd ratio.

es of ARF. The surviving patients received follow-up care for a mean of 476.6±374.6 days (27 to 1,318 days). There were no deaths after discharge. The mean left ventricular ejection fraction after discharge was 44.4±16.0% (14.5 to 63.1%), and all patients were considered to be in New York Heart Association functional class (NYHA Fc) I or II.

We analyzed the risk factors related to death before ECMO and after ECMO. CPR time before ECMO (>20 min), left ventricular ejection fraction (<40%) before ECMO, and concentration of albumin (<3.0 g/dL) were related to death (p< 0.05). ECMO support time (>4.5 days), increase of Troponin I (>100 ng/mL), ARF, DIC, and complications such as bleeding were also related to the death (p<0.05, Table 2, 3).

DISCUSSION

Circulatory supporting devices such as IABP and VAD limit the effect of cardiogenic shock due to AMI. IABP is fast and easy to apply and increases coronary blood flow. However, its effectiveness could be reduced in cases of cardiac arrest or ventricular arrhythmia [1,2]. VAD can also be effective, but requires an additional surgical procedure, more time, and money, and is therefore unsuitable in case of an emergency. Recently, VAD that can be applied percutaneously has become available. However, additional equipment and procedures are required in order to apply a VAD [10].

Since the advent of the percutaneous approach for ECMO, it has shown good results and that it can be applied relatively quickly. Its usage has become popular. CPR with ECMO shows better results than CPR alone, especially in cases of cardiogenic shock. In 2008, Chen et al. reported that CPR with ECMO obtained better results than CPR without ECMO when CPR was required over than 10 minutes. Prodhan et al. reported similar results [11,12].

There has been debate about whether coronary reperfusion or ECMO support should be first applied first at the time of postinfarct cardiogenic shock. In most cases, there has been limited application of ECMO after medical treatment and coronary reperfusion with IABP support at the time of cardiogenic shock due to AMI [13]. However, in the high risk group, maintaining coronary and whole body circulation through aggressive cardiopulmonary circulatory support is helpful in advance.

In 2005, Burkle et al. reported that the results of coronary reperfusion after ECMO support showed a better prognosis in high risk patients who had ischemic heart disease [14]. In 2007, Vanier et al. reported that the weaning rate from ECMO and the survival rate were 100% and 80%, respectively, in patients who underwent coronary reperfusion after ECMO support [15]. In Korea, Rhee et al. [7] and Ryu et

al. [8] reported the results of ECMO support before and after coronary reperfusion in ischemic heart disease, however, there has been no report of ECMO support just before coronary reperfusion. In this study, we performed ECMO on high risk patients who had cardiogenic shock and identified an ECMO weaning rate of 70% and a survival rate of 50%, which were similar results to those of several previous studies.

There have been varied results in the weaning and survival rates after ECMO support. Rastan et al. reported a 63.3% weaning rate and a 24.8% survival rate after ECMO support in their study of 517 cases in 2010, and Bakhtiary et al. reported a 56% weaning rate and a 33% survival rate in 45 cases in 2008. There have been studies with weaning rates ranging from 40% to 100% and survival rates ranging from 25% to 80% [16-18]. It is necessary to analyze the risk factors and to reduce them in order to improve the rates of survival and ECMO weaning. Rastan et al. addressed these rates' relationships with age, DM, hepatic failure, Euro score, ARF, and lactate and cardiac enzyme elevation [16]. Zhang et al. reported a noticeable elevation of cardiac enzyme, in weaning failure group [19]. Bakhtiary et al. suggested a relationship with lactate concentration, pulmonary arterial hypertension, DM, and IABP between waning group and weaning failure group [17]. Recently Chen et al. claimed that CPR time was closely related with the results of ECMO support [11]. This study identified that CPR time before ECMO support,, which consistent with the argument of Chen et al., and left ventricular ejection fraction before ECMO support had significant relationship with successful weaning from ECMO. We therefore think that early ECMO application should be considered in high risk patients who have reduced cardiac function. Analysis of cardiac enzyme showed results similar to those reported by Rastan and Zhang et al. Troponin I levels had statistical significance, whereas CKMB levels did not. Continuous monitoring of elevated cardiac enzymes may reveal their relationship to the death rate during or after ECMO support. Previous studies have reported that complications such as bleeding during ECMO support, multiple organ failure, and ARF may contribute to an increased death rate [7,8,20]. In this study, such complications contributed to an increased death rate as well. Decreasing the incidence of major complications would be helpful in improving the survival

rate in the future. Nevertheless, factors such as the site of the coronary artery lesion, the method of coronary reperfusion, three-vessel diseases, and the existence of a left main branch lesion did not influence the survival rate. We additionally inserted IABP in the 14 cases which had lost arterial pulse waves, but there was no meaningful difference in survival rates between the group with IABP and the group without IABP. Nevertheless, ECMO support with IABP could help to raise survival rates by recovering the arterial wave, decreasing afterload, increasing coronary blood flow, and weaning ECMO support [17] as has been reported by Bakhtiary et al. [17]. IABP should be applied during ECMO support if there is no contraindication to it.

Short term results are usually satisfactory after discharge. Studies have reported no differences in survival rates between immediately following discharge and one year after discharge. This study also showed no deaths immediately after discharge, and a good clinical course in all cases [11,20].

CONCLUSION

In this study, we analyzed the short-term results and risk factors related to death when ECMO support was applied before coronary reperfusion therapy in cases of postinfarct cardiogenic shock. Study limitations include a small study group, retrospective study, and the possibility of selection bias from nonrandomized study design. Coronary reperfusion therapy after ECMO support showed clinically significant results and good short-term results after discharge. In the high risk group, early ECMO support before coronary reperfusion procedures, correction of risk factors, and minimization of complications would result in improved clinical results for cardiogenic shock due to AMI. Long-term clinical applications of ECMO require further study.

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